UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/991,184 | 11/16/2001 | Juerg Zimmermann | 4-30096B/C1 | 8575 |

1095 7590 06/02/2004

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| O SULLIVAN, PETER G | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1621 | |

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/991,184 | ZIMMERMANN ET AL. | |
| | Examiner | Art Unit | |
| | Peter G O'Sullivan | 1621 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-44* is/are pending in the application.

4a) Of the above claim(s) *17-21,23-27,29-33 and 35-43* is/are withdrawn from consideration.

5)☒ Claim(s) *28* is/are allowed.

6)☒ Claim(s) *16,22,34 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 16-44 are pending in this application which should be reviewed for errors. In response to the restriction requirement applicants elected with traverse the invention of Group I, claims 16, 22, 28, 34 and 44. Claims 17-21, 23-27 and 35-43 are withdrawn from consideration as embracing non-elected subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 44 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating restenosis using free compounds or alpha or beta salts, does not reasonably provide enablement for all crystalline forms of applicants' methane sulfonate salts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicants' claim 44 claims a method of treating restenosis using methane sulfonate compounds of formula I which are non-hygroscopic at 25 degrees centigrade and at relative humidities up to and including 93 percent. Applicants' only crystalline form shown to have these characteristics is the beta form, but applicants claim all possible crystalline forms having them. Undue experimentation would be required to make and/or use other crystalline forms. Yu et al., US 5,985,893 disclose: "It is important to note that there is no reliable method to predict the obserbable crystal structures of a given drug or to predict the existence of polymorphs with desirable physical properties" (Col. 2, ll. 8-11).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

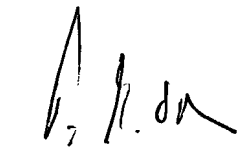
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16, 22, 34 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al., US 5,521,184, in view of Bilder et al., Cardiovascular Drug Reviews, Vol. 14, No. 4, pp. 380-399. Zimmermann et al. disclose N-phenyl-2-pyrimidine-amine compounds of formula I useful in the treatment of tumors and atherosclerosis for example (s. Col. 4, top). . Zimmerman et al. specifically disclose applicants' free base compound as example 21. The instant invention differs from the teaching of Zimmermann et al. in that the applicants' specific methanesulfonate salts are not exemplified, nor is the specific treatment of restenosis taught. Zimmermann et al. however disclose the compounds of formula I may be in the form of a free base or as salts with, for example, methanesulfonic acid (s. Col. 3, middle) and

additionally disclose: "Some of the compounds of formula I wherein R4 and R8 are hydrogen inhibit not only protein kinace C but, at a concentration IC50 as low as approximately from 0.01 to 5 micromol/liter, especially approximately from 0.05 to 1 micromol/liter, also certain tyrosine kinases such as PGDF-receptor kinase or abl-kinase, for example v-abl-kinase. Compounds of formujla I wherein at least one of the radicals R4 and R8 is other than hydrogen and is, for example, lower alkyl, such as methyl, are especially selective for the above mentioned PGDF-receptor and abl-tyrosine kinases and inhibit protein kinase C virtually not at all. (Col. 6 and 7, bridging paragraph). Bilder et al. is relied on to disclose that some phenylaminopyrimidine compounds are known to inhibit PDGFr tyrosine kinase with nanomolar potency and that atherosclerosis and restenosis respond to relatively less selective PDGFr TKI's. It would have been prima facie obvious at the time the invention was made to one of ordinary skill in the art to make methanesulfonate salts of applicants' compounds' and to expect them and the free base to treat restinosis.

Claim 28 is allowable. Hutchings et al., US 6,048,866, is cited as state of the art only.

Any inquiry concerning this communication should be directed to Peter G O'Sullivan at telephone number (571)272-0642.



PETER O'SULLIVAN
PRIMARY EXAMINER
GROUP 1200